WO 2004/041205 PCT/US2003/035139

## SEQUENCE LISTING

<110> DE CROMBRUGGHE, BENOIT AKIYAMA, HARUHIKO

<120> HA4, A NEW OSTEOBLAST- AND CHONDROCYTE-SPECIFIC SMALL SECRETED PEPTIDE, COMPOSITIONS AND METHODS OF USE

<130'> UTFC:772WO

<140> UNKNOWN

<141> 2003-11-04

<150> 60/423,690

<151> 2002-11-04

<160> 3

<170> PatentIn Ver. 2.1

<210> 1

<211> 735

<212> DNA

<213> Artificial Sequence

<220>

<221> CDS

<222> (1)..(735)

<220>

<223> Description of Artificial Sequence: Synthetic Primer

<400> 1

atg cac ccc caa ggc cgc gcg gcc ccc ccg cag ctg ctc ctc ggt ctc 48
Met His Pro Gln Gly Arg Ala Ala Pro Pro Gln Leu Leu Gly Leu

1 10 15

ttc ctt gtg ctg ctg ctt cag ttg tcc gca ccg tcc agc gcc tct 96
Phe Leu Val Leu Leu Leu Gln Leu Ser Ala Pro Ser Ser Ala Ser
20 25 30

gag aac ccc aag gtg aag caa aaa gcg ctg atc cgg cag agg gag gtg 144 Glu Asn Pro Lys Val Lys Gln Lys Ala Leu Ile Arg Gln Arg Glu Val

gta gac ctg tat aat gga atg tgt cta caa gga cca gca gga gtt ccc 192 Val Asp Leu Tyr Asn Gly Met Cys Leu Gln Gly Pro Ala Gly Val Pro 50 55 60

ggt cgt gat ggg agc cct ggg gcc aat ggc att cct ggc aca cct ggc 240 Gly Arg Asp Gly Ser Pro Gly Ala Asn Gly Ile Pro Gly Thr Pro Gly 65 70 75 80

atc cca ggt cgg gat gga ttc aaa ggg gaa aag gga gaa tgc tta agg 288

Ile Pro Gly Arg Asp Gly Phe Lys Gly Glu Lys Gly Glu Cys Leu Arg

85 90 95

gaa agc ttt gag gag tcc tgg acc cca aac tat aag cag tgt tcg tgg 336 Glu Ser Phe Glu Glu Ser Trp Thr Pro Asn Tyr Lys Gln Cys Ser Trp 11/9

110 100 105 agt tcg ctg aac tat ggc ata gat ctt ggg aaa att gcg gag tgt aca 384 Ser Ser Leu Asn Tyr Gly Ile Asp Leu Gly Lys Ile Ala Glu Cys Thr 120 ttc acg aag atg cgc tcc aac agt gct ctg cga gtt ctg ttc agt ggc 432 Phe Thr Lys Met Arg Ser Asn Ser Ala Leu Arg Val Leu Phe Ser Gly tca ctt cgg ctc aaa tgc agg aat gca tgc tgt cag cgc tgg tat ttt 480 Ser Leu Arg Leu Lys Cys Arg Asn Ala Cys Cys Gln Arg Trp Tyr Phe 155 150 aca ttt aat qqa gct gaa tgt tca gga cct ctt ccc atc gaa gcc atc 528 Thr Phe Asn Gly Ala Glu Cys Ser Gly Pro Leu Pro Ile Glu Ala Ile 165 170 atc tat ctg gac caa gga agc cct gag tta aat tca act att aat att 576 Ile Tyr Leu Asp Gln Gly Ser Pro Glu Leu Asn Ser Thr Ile Asn Ile 185 cat cgt act tcc tct gtg gaa gga ctc tgt gaa ggg att ggt gct gga His Arg Thr Ser Ser Val Glu Gly Leu Cys Glu Gly Ile Gly Ala Gly 200 ttg gta gat gtg gcc atc tgg gtt ggc acc tgt tca gat tac ccc aaa 672 Leu Val Asp Val Ala Ile Trp Val Gly Thr Cys Ser Asp Tyr Pro Lys 215 gga gac gct tct act gga tgg aat tcc gtg tct cgc atc atc att gaa 720 Gly Asp Ala Ser Thr Gly Trp Asn Ser Val Ser Arg Ile Ile Ile Glu 230 235 735 gaa cta ccg aaa taa Glu Leu Pro Lys <210> 2 <211> 244

<212> PRT

<213> Artificial Sequence

<223> Description of Artificial Sequence: Synthetic Primer

Met His Pro Gln Gly Arg Ala Ala Pro Pro Gln Leu Leu Leu Gly Leu 10 Phe Leu Val Leu Leu Leu Gln Leu Ser Ala Pro Ser Ser Ala Ser 25 Glu Asn Pro Lys Val Lys Gln Lys Ala Leu Ile Arg Gln Arg Glu Val 40 Val Asp Leu Tyr Asn Gly Met Cys Leu Gln Gly Pro Ala Gly Val Pro 55 Gly Arg Asp Gly Ser Pro Gly Ala Asn Gly Ile Pro Gly Thr Pro Gly Ile Pro Gly Arg Asp Gly Phe Lys Gly Glu Lys Gly Glu Cys Leu Arg 85 90 Glu Ser Phe Glu Glu Ser Trp Thr Pro Asn Tyr Lys Gln Cys Ser Trp 100 105



Ser Ser Leu Asn Tyr Gly Ile Asp Leu Gly Lys Ile Ala Glu Cys Thr 120 Phe Thr Lys Met Arg Ser Asn Ser Ala Leu Arg Val Leu Phe Ser Gly 140 135 Ser Leu Arg Leu Lys Cys Arg Asn Ala Cys Cys Gln Arg Trp Tyr Phe 150 155 145 Thr Phe Asn Gly Ala Glu Cys Ser Gly Pro Leu Pro Ile Glu Ala Ile 170 Ile Tyr Leu Asp Gln Gly Ser Pro Glu Leu Asn Ser Thr Ile Asn Ile 185 His Arg Thr Ser Ser Val Glu Gly Leu Cys Glu Gly Ile Gly Ala Gly 205 195 200 Leu Val Asp Val Ala Ile Trp Val Gly Thr Cys Ser Asp Tyr Pro Lys 215 Gly Asp Ala Ser Thr Gly Trp Asn Ser Val Ser Arg Ile Ile Glu 230 225 Glu Leu Pro Lys

gaattcggat ccagacaatg agaaggtaac aatacaaagc ttcttttggg gaagtccagg 60 tactttattc agttgcaaat tagcaaggct caagctcagt ctctggcctc ctagtgggcc 120 atcttgctct attttttct ttgtgaaaaa acacagactg aacccctacc ccagattaga 180 accggatctg gaccctttca atcattagtt agtgggtcct tccattttac catggcataa 240 gaattagaag taactggatg ccagnggcaa tccgctgcag actgaccttt aatatcagtt 300 tgcaaaaaat ttagaacaaa taaggcaaag gcaagatgtg cctttggtga ctttggggga 360 tataactgcc cctgttttgt ctaaaaaggc cagaaactct ctggaagtgg aggctgtgct 420 ctaaattaac ttgctaggta attaagaatt ttagctatct acaatatgaa tctctaatat 480 tggactaaat attagaccag tccaagattg aataactggt cacactgaag aaaagagaaa 540 aatcattatg actctattaa atgactaatc ttactaagtc agattatagt ctctgatgtt 600 cttttgccat aaagttaaaa ggcttgaagc tagtccaaac tagaaaaatg gcaagcaaag 660 atgggtctaa aacatgtacc caatttagtt tcctagtcac ttcaatcagg gcactgagtc 720 aactcacctg ccagctcatc acacgaatta accatcatgc ttctatagca ttctgtggag 780 agaacctatg tttttccctt ccctaataag gtagcagttt aggataaaac cataagccaa 840 taagtagatc tttttaagat actataaagc atttattaaa ttctttgaca tctaaatttc 900 aaaattcaaa aataaaagta tgatttaaat agtgtgcacg ggaatgtact aaataatatg 960 cacggggata taatttcccc cttctttgtc ttttaagaag ctaaagtttt aaagtttcac 1020 aatatctagt ccttagaatt aataacttgt tgacaaaaca tctcaaatac ttgactgtat 1080 tcatgtaaca aaggcagtga ctaattgcac tttcaattgt ttttcttaag gagcagttgt 1140 aactagaaag cttgaaaagt tattaatagt cacatgtgca taatttattt atttactaga 1200 aataagagta tttatttgca gcaatttatt aagtaaaggt cctcaagaat taacactatt 1260 atgtggaaac aagtagtaac tgaggacact aagaggaaag aattatacat gcacaatttt 1320 caagaatact aaaatattat cttaaaccat aactgctttg aatatacaaa gaacaaggtt 1380 atatattcaa totatottat atgtacgaco tatagactgo otgagatata aatttagoat 1440 ggcattgttt taagatgtcc aggcaatcta gaacaattta ttaaatgtct aaaaaccacc 1500 ttcttaaaag gacagcattt tttttctatg agttgtatac gcataagcaa ttgcaaattt 1560 qagaattaat agcatctgag ggacgaacaa tcttaagtaa ttgtgagctc tgagatataa 1620 cattgactat taatatacaa attaaggttt gattgttcag cattttaaaa caccatctac 1680 tqatctaatt cacatgtact tacatctcat ataggggttg ttttcaaaca caataattgg 1800 gatgtatgca tgtatgaatt tatagaagat acaaaagcat gtataaaaac aatttttaac 1860 ttatctttgg gatattgatt gtcaatctat ttaaaatgat ggtatgtcat aggtcaatta 1920 ttaatatttt gtaataacca aataaattgc tgtattgaac aaggaacata cacttagtca 1980 ggtttgnttt ttgttttttt gcttttttgn tttgtttntt tttttttttg gnttttcgag 2040 acagggtttc tctatagccc ttggctgtcc tggaactcac tttgtagacc aggctggcct 2100 cqaactcaga aatccacctg cetetgeete cegagtgetg ggatcaaagg cgtgegeeac 2160 cacgcccggc tattagtcag gtttttaaga cacaattttt ttttaaaaaa aaaatacacg 2220 aatatacatt acaattettt attagtacca cagtggttee aataggatge tgaaactgta 2280 ttttgaggtg aaaaccacct caatcttggc tgcctgccct cggccttcct ctcaggcana 2340 agaggetgaa ggcancecaa tetgttgtag accanaaaac centgeegag tettagtggg 2400 aaaaatatgg aggctcatgg ggcaaaggtg aacgcngccc tctcctgagt tcgctgtaaa 2460 gccacctgct ccttggcggc ctcttgtacc actatagctc tgggaaactg tgtgtctcaa 2520 ggccccaccc cacagcagcc agcagctagc tggcttcaca tgggtcaatg atcggctggg 2580 aggatgagaa aaatgacttt acaataatgt tttctcttgc caaagaattg ttttgagcac 2640 agctaatatc taattaccat tgattgtaat taataacaat tataaaagct ttctttattt 2700 tetgtaaage ettetgtagt aaactaaaac eetaagtaat aaaaagatat tgeetetgag 2760 tcttttgggt gagagcaagg atttaaagta aacttctctt gagaggcatt agctaataaa 2820 atattttcca cttaggaaac aatatacact gaaagattaa aactcttggc ttcttgtata 2880 gaagcagaaa tgataaaaat ttctcacata atgtagatca atatttagcc atactagagg 2940 ctaaatattc cagtngttnc anactcacta gaagcaaaac ctttacaatc attaagangc 3000 aaaggagaga gaaaaagaaa caaactttca gatctataat aactatataa aaggtaggca 3060 agccagattg taatgccttg ataaattata cagtctgatt gaccctttat aaactctaaa 3120 tttgaacttt attaaaacaa catctggcta gatccgtaaa ggtgctcttt tagctaaaag 3180 aatatctcct ggtttgcaag acaaaggaaa gtcacacaaa ccgaacagaa gctgctctga 3240 gcttagttcc tcttgccatg aggacatata ttagaattac taagtttctt ttgcaccatt 3300 aactttggga aagtaaaact ccattttaaa acaatttatc actttcggaa tcaacattaa 3360 aactttacta atacattgcg aaatttggcc tgctgtgcca cgtgcttgag aagactcctg 3420 agttgccaat tttaaggcta accttctgtt accaatgtaa caattattta atcttaacca 3480 ataacttatg agctgattgt gaaaacacgc agagcacatt accaataaaa aaaatgaagc 3540 agttacactt agaccaatca gagaatatta atttttctag ctacaatcat agaataaaag 3600 cactttatca tttgccaaat acattaataa cgattgcaga gaaccctcca ggaaaaaacc 3660 atttatcage ttttttacce caaaaccaag aggetgeaga etetetttt teetataaag 3720 aacagtttct ccagcagggg ccctcctgcg gtgtgctggt ttcctggtta aagcatgtgg 3780 ccactcttgg ctttgatgaa ccaccagata aagtttttta gccatcttta ttatccaaca 3840 taaaacatag aacattcatt cattctgact ggacacgaac atacatgaat tgaacatgtg 3900 aacggattgg tgcacccaaa cacaaaaaca caagagggca gagaacttct gctgtaaggc 3960 ccagagagaa caaagcagcg cacccctgaa atttctctct gcttctggga cattttcctc 4020 ccacatgatg cagtttctaa ctgtggccat ccacctgatt attaaatccc ttttattaaa 4080 ccctttcttt tctcacgcct aaaaaaagca acttcttgga gctgcggcta actgcctgat 4140 aaatttcact gctgaaacta agtgaattta gcgcgcaggt ttaacgcagt ttcaacttag 4200 cccataccaa ccttctccgg tacgaatttt ctttaattat tttcttcttc catggagctc 4260 caaaccagca atgettette caaatgteet etgetgttte ecagteeege gttggttege 4320 caatctgttg aggccagcca gcggcccaca tgtctgggtt ctagcctggg aggtatcttg 4380 gaatctggaa gagaagaggg aactaggcgg ctcgagagag aatggaacga taatggaacc 4440 aagacatcag tetgatcaag gtteaatttt aetatttgga gacaetgggt tatgaagtag 4500 agggaggggc ccattcctgc caaatcatcc ttggagtcca gtttcaggtg accacgtgtt 4560 ggctccggaa cagctaggcc gcaggtagca gcagtgggag tgacaggctc cacccctgat 4620 gctctnttag ccctaacagt caaacctgat cagccagatt tcaggctggg ggggaggtta 4680 attgagacag gaatttgctg tgtagccttt attgtcttgg aatttgctct gtaaactagg 4800 ctgtccatga actcacagag atctacctgc ctttgcctcc ctagtgctgg ggttaaaggt 4860 gttcaccacc accacctage ccataatete atattetate aagggattta ggttccataa 4920 atgcacttat cataagaggt tccaacagat ggaacacaac tacacagtat aaggtggact 4980 aatacatgtg tgtccttggt gaagaatccc ttatcttatg tcctttcatg tgcttgcttt 5040 atcaaaacat cctttcacct gtgtctgctt taggataaca ctccttcaca tgtttgccac 5100 agcaaagcac catcagacac gactgacttt ccaaagaacc cttaagtttc cacttcagat 5160 aggcatette ttetttaggt taagaaaatt ttttteetgt caetetgtgg aaaatatttt 5220

ctgtgcattt gacctgtgtt tcttctcctt ccttaattct tattttagat ttggtcactt 5280 cacagtgtcc cagatttcct ggatgttttg aaccaggagt tatttttaga ttgaacattt 5340 tetttgacet atgtatteat ttettetace atgtetteag tgtetgagat tetettttt 5400 aattettgaa ttetgttggt gaagettgee tetgtggttg etgtteaaat teetatatt 5460 tcatttccat atttccctca gtttggggtc tctttattaa ttctgttgga ggaagggggt 5520 ccaggagtca cctcacaaat cacatattcc caggattgat tgatcaggac caccggccag 5580 actcaggagc tgaactgtga tgtagagtca agatcctaca gggcttttaa agcctgagag 5640 ctataataac catctctgct aagttactcc accaatcata acttagggat agggctttct 5700 gtaggagcat gtctttgttg tgtacttatt ttgctcctat tggttagggt attcaactat 5760 ggcagaggac ttgcctcatc ttatattcat gtcttagctt gccaaccagg atatcagttt 5820 tccacataca tgtctctttc tgtcaagtag gatatcaagt tcccagggag gtcttggaaa 5880 cctaaacttt attctgcccc tactcaaaat ggaagtctta ttctaaatag gtacaggtgt 5940 ctctcttatg ttgggatcca tcccaagggc agcttaaaag gcaaatacta taaaggctga 6000 tacacaggtg cagaaagtgt tggtttctga gaacatccta gtaacagaag taacagcata 6060 tgagaaagtt teettgtgat attaggaaca geacaaactg gtaggttaga egggtaacag 6120 ttaccaagac cttaacaatc ccagttcctc tttcaggtct tgagtggctg tattcctttc 6180 cttccattgt ttgtgctttc atagacttct ttaagggatt taatgttttc tttttaagga 6240 cctctagcat acacatatag gctgtgttaa ggtctttatg tgtgcttcca gggtgtaata 6300 ctcagggcct gctgtgatag ggttggtggg ttctagtgga gacctatcgt cctggctgta 6360 attggttgtg caggggtagc ctgtaggttc ccaatgagtg tgtgcctgag ctggatgctt 6420 gggaaaaaca ttgagtgacg ggaggaaagt ggggggccag ggatctgtat gcttcactga 6480 agatgggtgc agaagcagcc tagggctgag actgaggggt tccactctga gaagcagagg 6540 gagaggtgaa gatctgcagt tagcccacct gcgtccctgc ccagtgtggc ctgtgggttc 6600 ccagggagtg ccggctggag ttgggggtgg agggtaggac agggcaatga gtgggggaag 6660 ggaatttagg aggggaagat ctgtgggatc caccagcgat gaggtggctg tggtggaagc 6720 cgctgcagga gttagcgcag agctcaggat gaaactaggg attgggcgtg gaggaatgga 6780 gggagcgtgg aggtcgcctc tccctctccc tggataggta ggtcacccat ttgcttcccg 6840 tcagagagtg cctaagagag ttggaggctg ctttcctggt tgaagttgga tagaactttt 6900 caaactatat taatctgatg tgaaataagc acgtgaaagt gaacctccag cactgaatgt 6960 tggctatttt ctaccagcct cagttcacct atgaatggag actccaggct gcatcgtccc 7020 ccacaggatt gccaagaggc cacgtgaaca aagctttaca ttttggagtt tagaaggggg 7080 taacactcaa acactatcga ttatttgagt cataggactc ttatagactg ttatattctg 7140 gctctctcca tttaataccc caaatgtcac ttttttttt tttttaata atgagcctta 7200 gttttttagg aatgaaggaa cacgaaggtg attcctgagg ccgagttaag acacgtgcct 7260 ctaagaaact caggagttgc ggtctccatt cccccaccac caccacctgt ggtttctgac 7320 cactgtcacc ctgcctggtc tctgctttcc tctctggttc tgcagcaccc cgcgggggtc 7380 tgggcgggcg gagctgcgga ggaggggcgg gctagacccg ggacccaggc ctataacagt 7440 atgcaaagct ceceggegte cagggggtgg gagggaaaaa ggaggeegge etcaatgaaa 7500 ggcgcattga tgcggcgggc tgcagggctg ggccagacgc tgagcagggt caggctcctg 7560 ccgacccctt tacctcctgc tccgcgcttc gcagccaccg cacaccatgc acccccaagg 7620 ccgcgcggcc cccccgcagc tgctgctcgg tctcttcctt gtgctgctgc tgcttcagtt 7680 gtccgcaccg tccagcgcct ctgagaaccc caaggtgaag caaaaagcgc tgatccggca 7740 gagggaggtg gtagacctgg taagtctgag agtcggtcct gacctcagtg ctggaagaga 7800 ggactcagcc aggatcgcac cggaagggca tcagtataga tggtggtggt gctgaccgta 7860 ggggtgagtg tagggcagca cgttaagaag cttgagtgcc tcagtgtcct gccttgtgta 7920 cctgtgtggg gacggatctg acgcacgcct gcagcagagt cttgaaccgc tacgggagat 7980 catgagaggt caccacatgc tccgacgtgg gtcaggtggg atgcccaaat ccgtgtagtc 8040 gcccagtaat ttctggctcc aggggaggcc accgttggga gaagtggggg atgctgtggc 8100 tgcaactgga gtagactgag ttagtcagtt gatttcaaaa gaaagcccga ggaagaccct 8160 aggccagctg gtcgcttggc cctgggccaa ggctgtgcaa cgtgtccttt gtgaggacca 8220 gtggccacga tctgccacgt ctgcctggag gagangctaa caacccccac aaagcatttg 8280 ttcagctaac ttgaagatta tgaatcactt tgtgtcatct ccctgggaaa tatgaactgc 8340 agtttactcc ttagaggacc acagcttgag ccaggagtgg tcagagactt tgaagctgaa 8400 ggggaaaaat gaaggcccca ctaggagccc ttccaaggac ccatttttgc ctgatctgtt 8460 taaaacagat gagcagtcag gtcttaacct gtgactgcca gtcaggaaca ctgtactcaa 8520 gctaagggga aggaaagcgc ttccaggaaa gcaaatatcc caagggcttt ctgagaggct 8580 aatctgtggg aaagtctgtt tgcttaaaac ctttccctct aaaagtcaat aaacctagtg 8640 gagggcagag agtttgtctg tcccactcaa gagccagcca tcgatagatt tgtagtcttt 8700 ggcacatcat aaacttetgt eettaaacca agetatatgg ttgtcaggca etgegataca 8760 taaaggacag gggacattta cttattttat tattattatt attattttag atttgaattt 8820 cttccactga cattctaagt tgagctaata aaccaagctc cttgacagct agttctaaac 8880

tgattcaaaa gcactggggg aaaatccctg ctgtttcacg cagcagtggt agggttttgt 8940 tgttttatgc tctgatatat aattttcctc cacaaaagca tactgtgttg gagctacagt 9000 tctattttga gtgcctaagt tgttaaaaaa aaaaaagtgc cacatgaatg tggctcgtgt 9060 gcagtttgcg tattatgaat gtgtagttaa gatacataaa atagtcattt ccccataaag 9120 ctagcatttt ccccctctaa ggattataca gtaccacaac tctaccccaa cttggaaaag 9180 catactgtgc tgccaggctc aggtgcatcc tgtagattgg atttggttct ggtgacagaa 9240 aaagtccaca cagtcattag gaaggtttcc acagattcta taaagcgact ttgtataggc 9300 gettteaaag egtgtettte aegeteecae tgaattetge eecetggtgg eeaacaeagg 9360 aaatggggcg ttgggtgagg gaatttgagc ttccattcac aggttttcat tttgttgact 9420 ttcactaatg attctaaata cctattggaa ctagcatttt aagttaagaa aagacaaaca 9480 tactctatgt agcatctttc ctgagaggaa tttagaaatt atcaaatcat actagaggaa 9540 tttacaacaa taaatgaaat gttaaagtaa aaaatttaat tggaattcat tgtgttttga 9600 aaagtctaac atcatccctg tttctatgtg aactaataca aggataagtg caggaattga 9660 taagcaacgc tcaaaatatt tccactgtag ctcaatggta gagtacttgc ctgatatgtg 9720 taaggttcta agttcaagcc tcattgatgt aatgtgaaca tgcatgctct ctctctct 9780 gtgtgtgtgt gttttgaggt gtggtcccat gtatcccaga ctaggcacaa atttgctgtt 9900 ttgacaggat cctaaactct gggtccctgc ctctgcttcc caggggaaag ggattacagg 9960 cacacgtgtg ctaccaactg ttaacttcat ggcaagaatg cttattatca tcttcatttt 10020 atttataagg aaatgggcac tgaaatgctg agtaaatggc ctggtctcat acatctaaga 10080 cgggatgagt ctagtattta aaaaaaaaa aaggttctag aatccacgcc tttaaattct 10140 acagcacaca gaaagaaaca acagaacaga gaacactagc gcttacagat ggtttgctag 10200 attattacac acctgctgag gacaggggat cacgtgaaac taactgggcc acagactcct 10260 cttgaggaag acagaatgga ctggagaagt tctacccact gcactttcct ctgcataaaa 10320 atgggaagag cagaggaggg gcacatccaa ctttagagat gttgcgatac aagacagcta 10380 ctgactgcta aagttttatt tcacaattat ttccctagca attattttag ggaaatcact 10440 caaaaggaaa aaaatctata tggccaagta ttctcattat attaatattt ataccaaaaa 10500 agagaaatac ccaaaaccaa gcattaaaaa tcttgtatag taatgtaaaa gttccaattt 10560 atggaaccaa gtcccttgat aaaatatggg attatgggcc tggcagtggt ggtgcatgcc 10620 tttctttaat cctagcactt gagaagcaga gagagttctg ggacagccag gggtacaagg 10680 caacaaaccc taaaacaaac aaataaaaag aaagggattg taagaagcta acatagaatg 10800 tcaggttctg gaggagaaat tttaaacacc cttaaaatga gttcgccata ataatccatt 10860 agaacacgga cgaggtgggt tagagggact ctgccagttt attaaaaata aacgcagctg 10920 tgatcatttg actctcacat actgtttatg tattcatgac tgtatttctt tatttactta 10980 ttttgtactg gggatcaaac cttgagcatc ctgcatgcca ggcaagagtt ctaccactgg 11040 actacctccc tatgccctac actgagtctg catgttaagt aatggtactg ccccctttc 11100 teetttgeac egtagtataa tggaatgtgt etacaaggac cagcaggagt teeeggtcgt 11160 gatgggagcc ctggggccaa tggcattcct ggcacacctg gcatcccagg tcgggatgga 11220 ttcaaagggg aaaagggaga atgcttaagg gaaagctttg aggagtcctg gaccccaaac 11280 tataagcagt gttcgtggag ttcgctgaac tatggcatag atcttgggaa aattgcggta 11340 agtaaagccc aaattataat aaagttgaag caaaatataa gagtttgtat aagtcattgc 11400 caaatttatt ttttattttg ttgttaaacc aaaggacctt aaattaaaag attcaggata 11460 ggtaatgtgc tgacttttta cttaaaaatt aatttaaaaa aatggtaacg tttcagctaa 11520 ttttataaag gcatttctaa gatagataat cactatttta taaagcaaac gcaaaaagta 11580 tagcttttct tttttcaaat tagacaggaa ccagtcttgt aaagtaactt taaattaatc 11640 taatacatcc tgctgtagct tcagagctaa aagtggaaga tgaacctaaa aattccacgt 11700 gactgggatc cctgctacgg gaagtccttt tgtccttggt cgccgtgctc agcttaaaac 11760 tgctgaaatt aggggaactg aagtcaatgc tagtgattta aaatagtgac gatggtgatt 11820 ctgtaatatt tgtgtaagga gaagcacgca aaatagcatg tcagggaggg cattttgatg 11880 aatgatecag ggactgttga gtggteetgt gattagtget ttgteteeaa gaggeecagg 11940 gtgtagctga gggggagcat gcggagcctc gtgtgcataa ggccctcggc tggatgaagt 12000 gccattggcg agtgggggg ggggggagaa gagacagaac tgagaaagtc cgtgctgttt 12060 cegtatette ttttgatgae cacetetgtt tetgeeteet tagetataat ttggtgette 12120 atggttctgc ttaccatgac cacccggaaa acagaagctt attttcataa aactctaagg 12180 ttttaagttg tagtatggcg tcatccacgt ttttcatctc aacctcttct gctctatttt 12240 aaaagttcaa gaattgcctt gattctgtgt gacaggtttt tcatctagct accacatttt 12300 ggttatacac acacacaca acacacatat atatatat attaaagaaa gtgtgatttg 12360 aatgatgact gttatttcaa catttgacaa tggtggactg ccttcttatt cacagttatt 12420 caatagaagt tgccattttc cccccaaagc tgtcccttta tggttcctgc tttttttggtt 12480 tggtttttta ttttttggtt tttggttttt tgagacaggg tttctctgtg tagccctggc 12540

tgtcctggaa ctcactttgt agaccaggct ggcctcaaac tcagaaatct gcctgcctct 12600 gcctcccgag tgctgggatt aaaggcgtgc gccaccaccg cccagcggtt cctgcattat 12660 taaaacacca tgatttttag cagtggttac caatgaatac ggaaatgttc tgcaaggaag 12720 agattgtagg tcataagcca atgtacagat tttgtgaaga ccagctagaa ggaagaaaac 12780 aaggetaget ettattaetg tgetgtteag gteatttgte taetgtgege tgttgeteaa 12840 aagaaagttg agcctggtgt ggtgactcag aataaatctc agtattcagg aagtagagac 12900 cactggaaac ctctggagtt gaaggccatc cttggctaca tagctatttc aaggccatct 12960 tgggctactg gaaaccccga ctaaaacaag aacaaccaca accaccacca taaccaccac 13020 ccaaaaggat ggagagagtg aacataatcc atcccaacag atatccacca acactctagc 13080 atgccagcgc cgtgagggcg gggcttcctt tgtgtgaact tttgtatcca accqtctaac 13140 atagagttga tattcagtgt ttttcaatag aaaaaaatac ataggtttgt tagctaaaag 13200 tactgaagac tagctgtttt tgaagataaa taggaagtga aataaaacca tctaagaaag 13260 ccagaagttg gttttcttgg ctcttgtatc aatctgataa gtaatcttta tccctctata 13320 aaatttaaga atgttaaaga catgggggag aaggcaggta aaaattcaca gtgtattttc 13380 agtotottat titactotot cotatgocot otocaccaat tictottota titootococ 13440 ctcccctcc ccctcccact tcatgtactt ccttaaaact cgaccaggtc cacttggtgc 13500 tgtctatgtg tgtctctggg aacataggga gcctctatgg gtctcatctc tggagaaaac 13560 agattttgtc tccctagcag ccatcagttg ctcacagetc cacagetagg ggtggggetc 13620 catgggctct tccccatgca tgctgggagt ttggttgatt ttgtacaggc cttgcacgtg 13680 taacctattg tgagttcata tgtgccatgg ccctgttgtg tctggcaaat tctgtttcat 13740 tgcaggtgtc tactacctca caatcccccc cgccccactc cccttgtagt ctctgaacat 13800 tgaccagatg tcgagtctct gccttaatct ccatctactg caaaaggagg gttctatgat 13860 gagggttgaa gaaatgtgtt aatttatagg tattaaaaaa gaaaccttag gggccagttt 13920 attactatgt ccttttaaca gaataatagt attactttct tctctaggac cttatgagct 13980 ggttggatat ggattttggg tccagtgaac tatagcaggc ctgagtttca tttttttggt 14040 tgaactggct tttaacccaa tcactaaata caactattta atgaccccct aacacttgag 14100 ccaccactgc actagtggca ccaccgctat cacagttcac agggtgccca gctgggtaaa 14160 acacttcatt actttttcct tggcagcatg cactgagcct tccagcacta tgaaagttaa 14220 ccaggaaggg cgaatcttct atgtcactga cagcttaatt ttccacatcc tatgacttaa 14280 gtatgtggga ccatcagaaa taggagtatt attcagctgt aaagaaaaag gaaattatga 14340 aattcacacg taaatgggtg gaagctgaaa atattcattt cqaqtqaqat ccctccaaac 14400 ccaggaagac acagaacgaa gcatgttete teteatgeat ggaegeeage tttgaagett 14460 tagatatgca tatttaaatt aggctatagt catagaagtt atcaagttag taaggggagg 14520 gggtacaatg caggcagtgt ggaggaggaa agggaattac cagcacaggt tagatgggag 14580 ggcaggagag gggacagtgt ctgagcacgg atatacaata ctgaagacct ttgaaaaaag 14640 cctactactg cagaagcatc ctaaactatg tacatccata tttgtaaaag gagctaaatg 14700 gtgtttccct agacatcata gactaccaag taaaaaagta ccagatatgg ggtacctctt 14760 tttgagttat tgatcagtgg agtctcaaag gcctccccaa atttcagact gtggtcatta 14820 ttatgggtta gcctccataa cttgatggtt gaagaaactt tttaatcaaa atgaaaaatg 14880 tctggctgtc ttgctgccct ggcaggagtg tacattcacg aagatgcgct ccaacagtgc 14940 tetgegagtt etgtteagtg geteaetteg geteaaatge aggaatgeat getgteageg 15000 ctggtatttt acatttaatg gagctgaatg ttcaggacct cttcccatcg aagccatcat 15060 ctatctggac caaggaagcc ctgagttaaa ttcaactatt aatattcatc gtacttcctc 15120 tggtatgtat aatagtggtg tttctgagtg agcctcaaat ctgcctaaga ggttgtttga 15180 tttccactgt cacagtgggt atctaacctg ttagaaataa acctctagct ggtccatagt 15240 cctctagctg gtctctcctc cctggactgc aattcacata attttacaga tcttttttc 15300 aaagggtata gatgctaggg tgtaatctct gatcaaggga ctcagaatct ctggtgtaag 15360 gctccagaat gtttatctta aaaacaaaat aaaacaaagc aaacaacaac aacaacagaa 15420 accgtagttg tgataatatg ccccaaaatt gaaaatcaat gataagttag aaacggcaag 15480 acagccagga attctataca gcagtggctt tggttctcag ctttggcaat acaacqqqtt 15540 catctgagaa acttgaaaaa aagattcctg ccctgggtac tgctcctcca ggaagattca 15600 attaatgggg atttgatcat tacatcgttt gcattgcagt gaggctgatg gtagacccac 15660 acctgtctac agtctgttgg cttcaggctt aagtagactc atttctaggg tataaggggt 15720 caaggeettg gggacaetta agtattgetg geatgeattt teagetagea tggtgtagae 15780 tactagacaa tttaagtggg actgtggact caccacctac ctcccactgt agaagaggtc 15840 tgggtatgct gtagccaggg agggcagagt cctttagttc tgtattcctg ggcctcagtt 15900 gaactgcatt cacttcagct aaggtggaaa cctgacaggg cacataagta cctcaaagtc 15960 aaccaggtag gaaagctaaa tagccacggc actacaatgt caagagccat tttcttcaag 16020 aatcagccac ctccagtaag gaaaggaatc gcactaagca cagacatcga aagtaatgcg 16080 actctctgcc tgtttcagtg accaaccatg aaatctttct ttagatgtga gtgaagaact 16140 ttggtaaatt ggaatgcaag atgtatgtta gaatgtgaga gcccagaggg tatgcgtagg 16200

atacagtatc aaaccaaagc agagcaaaaa gcagaacaga aaacagaaca agccaggtgt 16260 ggtggcgcac acctttaatc ccagcacttg ggaggcagag gcaggcagat ttctgagttc 16320 aaggccagcc tggtctacaa agtgagttcc aggacagcca gggctataca gagaaaccct 16380 acaaacaaaa aaccagaaca aaatgtcctc tttaatataa tcatcctatt aaagggtcag 16500 tgaggtggct tagcaggtag aaggcactct cccacccct cagagtctga ggacctgtgt 16560 ttgctccctg ggacccatat ggtagaagga gagaaccaac ccttgtaatc agctgtcctc 16620 taatcttcac atgtgcactg tggcacgtgt gtatccacac ctacatatac acactagata 16680 gtaggtaggt aggtaggtag gtaggtaggt aggtgcatac atacatacat agatgtaatt 16800 tttttgccaa aaataagaat ctatttaaag tggattcaca gattgaaggg atggtatgag 16860 attaagctag aatttctttt tctcatatag aagtcctatc ttggatttga atagcatcta 16920 gggatccacg ttgaaaagga ctttctttaa aaagacttgc atatcttgat ccaggctctg 16980 gttcaggtct cttccaaagt tgggaagtct taaaagttgg aagtgtaggc ttcccatatg 17040 tttgggtaaa ttgttctttg gttctaagta tctagaacac gttttggttt gagagcactg 17100 cctatagcat agcaatcatg gaaatgcctc caaaaatgtc tatgtatcaa ctaaaaaaat 17160 gagacettta ttacgaaate atcaggtact agaattttta attagetttg cattaaacag 17220 aattataacc tgatttccta tagtaaatgc aaaattagtg gttttgcttt ttgttcttgg 17280 gttgtgactg gctctgtttt gcagtggaag gactctgtga agggattggt gctggattgg 17340 tagatgtggc catctgggtt ggcacctgtt cagattaccc caaaggagac gcttctactg 17400 gatggaattc cgtgtctcgc atcatcattg aagaactacc gaaataaagc ctctgacggt 17460 ttcagtccct gcctcgttgg ctttttaaat caagcccttg agtggttcat ttaaatgaca 17520 tttaagaaat cacttaaatg aagtgctcag ctgaatgaaa aagcaaagtt aaatatgttt 17580 acagaccaaa gtgtgatctc acacttaaaa atctagtatt aaccatttta tttcagccaa 17640 agatggtttc aggatttttt tttcattatt attttttaag cctatatatt ggaatgccat 17700 tacagtattt agtatttcct tctataacat ataaaggtta tgtctttgta aggactgtat 17760 agaattattt tatatctgtt aaataaaatg cttctaaaac ctaagtattt gtttattcgt 17820 ttgattgtgt agccctggct gtcttgaaat ctgcactgta gaccaggctg gcctcaaatt 17880 ccgagatctg tcaaccttta tttcccatgt gctgagattg aaggtgtgca ccaccatgcc 17940 tagcaacttt attattttta aattgaagat tttgccactg aagttgaatt cctagtactt 18000 aacatatgtg aaattgaaca taaatctaaa ttttaactat tcatttagca atttatgaaa 18060 ttttagcaca tatatataac atggttctgt atcttgagat atatgaagac ataaggatgt 18120 ttatctgaca ggaatataac agtattttag gaatttttgt ctccttttt tttttattgg 18180 atattttctt tgtttatact ttaaatgttt tcccctttcc aggtctcccc ttcagaaacc 18240 cccattccat cccctgctt ctatgagggt gctccccca cccacccact caaatcttcc 18300 tgccccaccc agcattcccc ttaaatgcca aaaacagtct tttaaaagaa cagcattttt 18360 tettatgagt tggatatgta taaacaattt gcaaattttg agaatttett agttetaagg 18420 angaaggaac caatttttta agccaatttg ggaaagctcn tggnaaaatt actttaatcc 18480 cttnttaaaa tattncccaa atttaaangg cctttgggan ttantttcaa aacaattttt 18540 taaaaaaaat aacccgggtn ttaacagggn ncaacnaaat tttaaattta ntcntggggc 18600 cctgggaaan ccnngggang gggaaaaccc cnnnnnnnn nnnnnnnnn nnnnnnnnn 18660 agnetttttt teaanaagaa agggaaatgg aagetaeeaa taggtatgta tttattagag 18780 atacatctag agtctgcttt ttgtttaatt cttcaggaat tcaagacttt aagtaccctc 18840 aaagcttaca gtttntacgt tacctagcac gttttcagag agcagcacaa aggttaaaca 18900 aaccatttta catccatgtc attttgtaag tgcttgactt tgctgccaaa gtgaatacat 18960 gttatctaca gaattttatt ttctattgaa aacagtgcct gtatcccaag gagaattagc 19020 tttttttgat acagtggaaa taaaacaaac aaacaacaa taacaacac catgcatacc 19140 ttaaaataaa acagtaacaa caacaacaac acacacaca atcccttaag gtcaaaaact 19200 taaataactg ggccataaat ggatatatac tcaagtagaa tagcctctcc caaggcatgc 19260 cagccatcag tggatcccat tctggttcac acacctgctt gtgggttggc tggcccttta 19320 tgttcaaagg tgccccatc ctgctctgcc tttccttttg ccaacctccc caacttgcac 19380 cttctcttag tctcggttac ttttcaagct ccagttcttc acttttatct gccaactcca 19440 agaaagagga atgatgetee tteagagett geeetetaae tteeggttet gtaatteaaa 19500 tgggattaaa gttctcagcg gcatcaacct tcaccctact gaaatagtta caggcttgat 19560 gacactcctt ttgagttgct cctgttgaac attcctgctt ctcctaagat gtagacacag 19620 ttctctggcc tacctactgt gttctctttt gaccattaaa acctcaacat gtttatagta 19680 aagctccaag agttctcaag ttctggtctc agtctttcag cttgctcttc caattatact 19740 gataactcgc tgctcataac aggccacctc tgctaccacc cgccatactt ctctccaaaa 19800 taactteett caagteeage ceacegeest tetaaaatat tgeeeeggtt eettataage 19860

18/9

tgtaagtcac	catctctgat	accatcaacc	aggctgaagt	ctctagctct	tgactagata	19920
cttatcaaat	atagccttgt	tcccacaatt	cagaacgagc	tcttggtcta	aatttcttac	19980
cagtctacaa	tacagggtaa	gaactggctt	ctgtttatat	taattagccc	agctactgca	20040
ttgcactctt	tatttggatt	catttactcc	atcaaagtat	agcaatgtac	tttaaattgt	20100
		gctggtggac				20138